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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,286	FLYER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *5-13,15-23, 26-29, 31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,14,24,25 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 7/22/04 is acknowledged and has been entered.

2. Applicant's election with traverse of Group I (claims 1-8, 14 and 24-30), and species of SEQ ID NO: 1 in Applicant's said response is acknowledged.

The basis for the traversal is that all sequences sufficiently similar to SEQ ID NO: 1 should be included within the examination, and that if the claim recited a percent identity then more than one sequence would be within the claim.

Applicant's arguments have been fully considered but are not persuasive.

It is the Examiner's position that the SEQ ID NO are different sequences and require different searches. It is the Examiner's further position that if the claim recited a percent identity, the Examiner would still have required an election of species for purposes of searching. Applicant is reminded that if upon consideration of a search, if SEQ ID NO: 1 appears to be free of the prior art, then the search will be extended to another species.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 5-8 and 26-29 (non-elected species of Group I) and claims 9-13, 15-23 and 31-32 (non-elected groups II-VIII) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Upon consideration of the prior art, the search has been extended to include SEQ ID NO: 5.

Claims 1-4, 14, 24, 25 and 30 are currently being examined as they read upon SEQ ID NO: 1 and SEQ ID NO: 5.

3. Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NO for sequences disclosed in the specification (for example, page 46 at line 1 for SEQ ID NO: 1).

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: although inventor Flyer has initialed the changes to the declaration, he has not put a date by his initials to indicate when the changes were made.

5. The disclosure is objected to because of the following informality:

The use of the trademark PBLUESCRIPT has been noted in this application on page 27 at line 3. It should be capitalized or accompanied by the ™ or ® symbol wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 14, 24, 25 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed immunogen, pharmaceutical composition and vaccine thereof, recited in the instant claims.

The instant claims encompass (1) an immunogen comprising a peptide segment of at least 8 but not more than 14 amino acid units in length which segment comprises a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5 or a sequence differing from said sequence by not more than one amino acid residue and wherein said immunogen is not hsp65 protein, and vaccine or composition thereof, or (2) an isolated peptide of at least 8 but not more than 14 amino acid units in length and having a sequence differing by no more than one amino acid residue from a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5, and a pharmaceutical composition thereof. There is insufficient disclosure in the specification on such an immunogen and vaccine comprising said immunogen or on such a peptide and pharmaceutical composition thereof.

The specification discloses that the sequence of SEQ ID NO: 5 is found in M. bovis HSP65, that the peptides of SEQ ID NO: 2, 3 and 4 are derived from an M. tuberculosis hypothetical protein "Rv0341", that the peptide SEQ ID NO: 1 is derived from an M. tuberculosis hypothetical protein "Rv3808c", and the said SEQ ID NO have been found in association with HLA-A2 in mammalian cell lines infected with M. tuberculosis and are useful as an immunotherapeutic in the prevention and treatment of tuberculosis (page 14 at lines 17-21 and page 20 at lines 9-16). The specification further discloses that the peptides can be used for the prevention, treatment and diagnosis of bacterial infections, especially tuberculosis (page 14 at lines 10-12). The specification discloses that the polypeptides can be of any desired length so long as they have immunogenic activity in that they are able, to elicit in vitro or in vivo the activation of CTL against a presentation of TB-infected cells when such polypeptides are presented along with MHC class I proteins (page 16 at lines 10-18). The specification discloses that the immunogenic peptides may be part of an immunogenic structure via attachments other than conventional peptide bonds (paragraph spanning pages 21 and 22). The specification discloses that peptides can be modified at positions that bind MHC class I or at positions that interact with TCR on CTL (page 22 at lines 7-22). The specification discloses that the peptides may have up to 2 substitutions, so long as they have substantially identical antigenic activity (pages 24 at lines 25-28).

The specification does not disclose any immunogen comprising SEQ ID NO: 1, 2, 3, 4, or 5 or one comprising the SEQ ID NO differing by not more than one amino acid residue used as an immunogen or used prophylactically or therapeutically as a vaccine. The specification does not disclose any peptides or immunogens comprising SEQ ID NO: 1, 2, 3, 4, or 5 that have flanking amino acid residues.

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera, including peptides that are variants within the said SEQ ID NO or that have flanking amino acid residues of undisclosed identity, i.e., the recitation of "An immunogen comprising a peptide segment" is open to any length and does not necessarily include sequences flanking the said SEQ ID NO in the protein of origin. Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

8. Claims 1-4, 14, 24, 25 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and use the instant invention (1) an immunogen comprising a peptide segment of at least 8 but not more than 14 amino acid units in length which segment comprises a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5 or a sequence differing from said sequence by not

more than one amino acid residue and wherein said immunogen is not hsp65 protein, and vaccine or composition thereof, or (2) an isolated peptide of at least 8 but not more than 14 amino acid units in length and having a sequence differing by no more than one amino acid residue from a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5, and a pharmaceutical composition thereof. The specification has not enabled the breadth of the claimed invention because the instant claims encompass an immunogen comprising a peptide segment of at least 8 but not more than 14 amino acid units in length which segment comprises a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5 or a sequence differing from said sequence by not more than one amino acid residue and wherein said immunogen is not hsp65 protein, and vaccine or composition thereof, or an isolated peptide of at least 8 but not more than 14 amino acid units in length and having a sequence differing by no more than one amino acid residue from a sequence selected from the group consisting of the sequence of SEQ ID NO: 1, 2, 3, 4, and 5, and a pharmaceutical composition thereof . The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed immunogens/vaccines/peptides/ compositions can be made and used therapeutically or prophylactically. The specification discloses no working examples with regards to the use of the instant peptides of SEQ ID NO: 1-5 for immunization, prevention or treatment in vitro or in vivo.

The specification discloses that the sequence of SEQ ID NO: 5 is found in M. bovis HSP65, that the peptides of SEQ ID NO: 2, 3 and 4 are derived from an M. tuberculosis hypothetical protein "Rv0341", that the peptide SEQ ID NO: 1 is derived from an M. tuberculosis hypothetical protein "Rv3808c", and the said SEQ ID NO have been found in association with HLA-A2 in mammalian cell lines infected with M. tuberculosis and are useful as an immunotherapeutic in the prevention and treatment of tuberculosis (page 14 at lines 17-21 and page 20 at lines 9-16). The specification further discloses that the peptides can be used for the prevention, treatment and diagnosis of bacterial infections, especially tuberculosis (page 14 at lines 10-12). The specification discloses that the polypeptides can be of any desired length so long as they have immunogenic activity in that they are able, to elicit in vitro or in vivo the activation of CTL against a presentation of TB-infected cells when such polypeptides are presented along with MHC class I proteins (page 16 at lines 10-18). The specification discloses that the immunogenic peptides may be part of an immunogenic structure via attachments other than conventional peptide bonds (paragraph spanning pages 21 and 22). The specification discloses that peptides can be modified at positions that bind MHC class I or at positions that interact with TCR on CTL (page 22 at lines 7-22). The specification discloses that the peptides may have up to 2 substitutions, so long as they have substantially identical antigenic activity (pages 24 at lines 25-28).

The specification does not disclose any immunogen comprising SEQ ID NO: 1, 2, 3, 4, or 5 or one comprising the SEQ ID NO differing by not more than one amino acid residue used as an immunogen or used prophylactically or therapeutically as a vaccine. The specification does not disclose any peptides or immunogens comprising SEQ ID NO: 1, 2, 3, 4, or 5 that have flanking amino acid residues.

Evidentiary reference the Merck Manual teaches that a vaccine is a suspension of whole or fractionated bacteria or viruses that have been rendered nonpathogenic and is given to induce an immune response and prevent subsequent disease. Evidentiary reference Encyclopedia Brittanica Online defines vaccine as a suspension of weakened, killed, or fragmented microorganisms or toxins or of antibodies or lymphocytes that is administered primarily to prevent disease. Evidentiary reference Vordermeier et al (Scand. J. Immunol. 45, 521-526, 1997, IDS reference) teaches epitopes from hsp65 and from 38Kda lipoglycoprotein antigens of M. tuberculosis, and that it appears that production of large amounts of γ-IFN by the responding CTL line is of critical importance in protective anti-tuberculous immune responses. Vordermeier et al teach that peptide vaccination does not reflect a physiological way of CTL induction similar to that by infection or following vaccination with tubercle bacilli, and the instant specification does not disclose any therapeutic or prophylactic result using the said SEQ ID NO or peptides comprising the said SEQ ID NO with substitutions or flanking sequences.

As to the issue of "*comprising*", the specification does not disclose wherein the peptides constitute a CTL epitope and additional sequences that are not a T cell epitope. There is no guarantee that said peptide would bind to HLA and would be recognized by CTL, i.e., be a T cell epitope. The specification provides no evidence that the peptide of at least eight amino acid residues: (1) would bind to any MHC molecule, in particular to HLA-A2 when it is 8 amino acid residues in length, or when present in a longer peptide of unknown length and flanked by amino acid sequences not present in the antigenic protein of origin, (2) or would be recognized by CTL. In addition, the art recognizes that flanking sequences influence the processing and presentation of CTL epitopes (Eisenlohr et al, Shastri et al, Bergmann et al, Wang et al, Perkins et al, Theobald et al and Gileadi et al), that immunodominance can be affected by the context of the epitope within the protein molecule and that junctional neoepitopes can be created (Perkins et al) or that immunodominant epitopes can be completely silenced by contiguous sequences (Wang et al). An undue amount of experimentation would be involved in determining longer peptides from the many possibilities that would be capable of binding to HLA and being recognized by CTL. In addition, Anderton et al teaches that in vivo use of altered peptide ligands is unpredictable and dangerous in outbred human populations.

In addition, the art recognizes that for a peptide to be a T cell epitope, the length of the peptide is important for binding to HLA (along with the presence of anchor (or "motif") amino acid residues present within the peptide). The peptides that bind to class I molecules have a predominant length, i.e., a minimum of 8 or 9 amino acid residues for a class I MHC restricted T cell epitope peptide. A primary factor for this is that amino acid residues at the amino- and carboxy-termini of peptides binding to class I molecules interact with conserved amino acid residues in pockets ("A","F") located at opposite ends of the binding groove of the class I molecule, giving rise to a common orientation of the peptides in the binding site (Engelhard at page 14, column 1, lines 16-27.) Thus, the amino acid residues at the peptides' termini make a network of hydrogen bonds with conserved residues on the sides and bottom of the peptide binding groove of class I molecules. These interactions are important for holding

the peptides in the binding groove and for stabilizing the complex (Guo, et al at page 366, column 1 lines 1-10.) "...the preferred length (of the peptide) is determined by the minimum amount of peptide required to span the center of the binding site and optimize the interactions at the ends" , but that the predominant length is 9 amino acid residues (Engelhard at page 14, column 1, lines 23-27). The minimum length for a peptide to be a T cell epitope for class I MHC is 9 amino acid residues (Rammensee et al at page 182, column 2, last paragraph).

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4, 14, 24, 25 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

a. Claim 1 is indefinite in the recitation of "amino acid units" at line 2 and "amino acid" at line 4 because it is not clear what is meant. It is suggested that Applicant amend said claim to recite "amino acid residues" and "amino acid residue", respectively.

b. Claim 3 recites the limitation "one or more of said peptides" at line 2. There is insufficient antecedent basis for this limitation in the claim. Base claims 1 or 2 recite "peptide segment".

c. Claim 14 is missing the limitation "the" in front of "said immunogen" at line 2 and a comma after "8" and before "wherein" at line 2.

d. Claim 24 is indefinite in the recitation of "amino acid units" at line 1 because it is not clear what is meant. It is suggested that Applicant amend the claim to recite "amino acid residues".

e. Claim 25 recites the limitation "oligopeptide" at line 1. There is insufficient antecedent basis for this limitation in the claim. Base claim 25 recites "peptide".

f. Claim 3 recites the limitation "said immunogen segment" at line 1. There is insufficient antecedent basis for this limitation in the claim. Base claims 1 or 2 recite "peptide segment".

11. For the purpose of prior art rejections, the filing date of the instant claims 1-4, 14, 24, 25 and 30 is deemed to be the filing date of the 60/264,987 provisional application, i.e. 1/30/01, as the 60/255,292 application does not support the claimed limitations of the instant application. SEQ ID NO: 2-5 are not disclosed in the 60/255,292 application, nor the limitation recited in instant claim 1 "wherein said immunogen is not hsp65 protein", nor the limitation recited in instant claim 3 "at least 5 copies" in context of the immunogen recited in

base claim 1. Provisional application 60/255,292 does not disclose the limitation recited in instant claim 1 "wherein said immunogen is not hsp65 protein", nor does it disclose the limitation "at least 5 copies" recited in instant claim 2 in relation to the recited peptide segment in claim 1, nor does it provide support for sequences comprising SEQ ID NO: 2-5.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 2, 4, 14, 24, 25 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over SwissProt_42 Accession No P06806 in view of Mohagheghpour et al (J. Immunol. 1998, 161: 2400-2406) and Ruppert et al (Cell 74: 929-937, 1993).

SwissProt_42 Accession No P06806 teaches a protein from M. bovis and M. tuberculosis that is a purified 65kDa antigen that can elicit a strong immune reaction in animals infected with M. tuberculosis, and that the said protein is one of the major immunoreactive proteins of mycobacteria. SwissProt_42 Accession No P06806 further teaches that the protein is a HSP from the HSP60 family. SwissProt_42 Accession No P06806 teaches that amino acid residues 415-423 are a subsequence of the said protein, which is identical to SEQ ID NO: 5 (TLLQAAPTL) of the instant claims.

SwissProt_42 Accession No P06806 does not teach the isolated peptide TLLQAAPTL, nor in a vaccine or a composition comprising a pharmaceutical carrier.

Mohagheghpour et al teach importance of CTL in protective immunity against M. tuberculosis and further teach screening of a major target antigen protein of M. tuberculosis for subsequences of between 8 and 10 amino acid residues that contain the HLA-A201 binding motif and immunogenicity of the said subsequences in humans. Mohagheghpour et al teach the binding motif of HLA-A201 is taught by Ruppert et al (Cell 74: 929-937, 1993). Mohagheghpour et al teach that their findings are relevant for both vaccine development and adoptive imunotherapy. Mohagheghpour et al teach the peptides suspended in a pharmaceutical carrier.

Ruppert et al teach peptides of 9 or 10 amino acid residues in length containing the canonical anchors L or M in position 2 and V, L or I at the C-terminal position.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the HLA-A201 peptide binding motif taught by Mohagheghpour et al and by Ruppert et al to scan the sequence of the major 65kDa immunoreactive protein from M. tuberculosis taught by SwissProt_42 Accession No P06806 for subsequences possessing the binding motif and possessing the potential to be an immunogenic CTL epitope, i.e., to arrive at the sequence TLLQAAPTL, as taught by Mohagheghpour et al for another major target antigenic protein of M. tuberculosis, and to have suspended it in a pharmaceutically acceptable carrier as taught by Mohagheghpour et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a peptide that can bind to HLA-A201 and potentially be recognized by M. tuberculosis specific CTL since Mohagheghpour et al teach the importance of CTL in protective immunity against M. tuberculosis and that the finding of peptides that bind to HLA-A201 from M. tuberculosis antigenic proteins are relevant for vaccine development and for adoptive immunotherapy, and SwissProt_42 Accession No P06806 teaches that their 65 kDa HSP is one of the major immunoreactive proteins of mycobacteria. With regard to the limitation of "An immunogen comprising a peptide segment" recited in claim 1, the said peptide would be expected to be immunogenic for antibody production since it comprises the minimum of 6 amino acid residues known in the art to be the size of an antibody epitope. With regard to the inclusion of claim 14 in this rejection, the term vaccine must be weighed with the structural limitations of the claim. If the vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. With regard to the inclusion of claims 24, 25 and 30 in this rejection, the peptide TLLQAAPTL is identical to SEQ ID NO: 5 of the instant claims and therefore it has a sequence differing by no more than one amino acid residue from SEQ ID NO: 5.

14. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over SwissProt_42 Accession No P06806 in view of Mohagheghpour et al (J. Immunol. 1998, 161: 2400-2406) and Ruppert et al (Cell 74: 929-937, 1993) as applied to claims 1, 2, 4, 14, 24, 25 and 30 above, and further in view of U.S. Patent No. 5,662,907A.

SwissProt_42 Accession No P06806, Mohagheghpour et al and Ruppert et al have been discussed supra, hereafter, "the combined references".

The combined references do not teach wherein the immunogen comprises at least 5 copies of the peptide.

U.S. Patent No. 5,662,907A discloses that immunogenic peptides can be introduced into a host, including human, as a homopolymer of active peptide units, especially when being used in a vaccine composition (especially column 12).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a peptide/composition thereof comprising a homopolymer as disclosed by U.S. Patent No. 5,662,907A, including at least 5 copies of the immunogenic peptide taught by the combined references.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a more effective immunogen as disclosed by U.S. Patent No. 5,662,907A and because one of ordinary skill in the art at the time the invention was made would have been aware that increasing the size of the peptide would increase the half-life in circulation as pertains to digestion by proteases in vivo. In addition, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07.

15. It is requested that Applicant correct the spelling error at the last line on page 46 of the specification, i.e., "hsp56" to "hsp65". Applicant discloses on page 20 that SEQ ID NO: 5 is from Hsp65.

16. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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